

Notice of Allowability	Application No.	Applicant(s)	
	10/658,959	JOHN ET AL.	
	Examiner	Art Unit	
	Zinna Northington Davis	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to the Amendments filed October 18, 2005, November 29, 2005, and February 28, 2006.
 2. ☒ The allowed claim(s) is/are 1-15, respectively.
 3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
 5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
 - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|---|
| 1. <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input checked="" type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____. |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO-1449 or PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____. |

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Bradley Crawford on February 28, 2006.

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

Group I: Claims 1-14, drawn to a chemical compound, a method of preparing, and a method of treating using a compound of formula (I) wherein R_c represents heteroaryl or heterocycloalkyl.

Group II: Claims 1-14, drawn to a chemical compound, a method of preparing and a method of treating using a compound of formula (I) wherein the compound is not represented in Group I.

3. Inventions I and II are related as products which share an alleged common utility of treating but the common utility is not linked to a substantial structural feature. The products in this relationship are distinct if either or both of the following can be shown: (1) that the products encompass embodiments that are not required to perform the common utility or (2) that the products as claimed can be used to perform another utility. In this case, the products encompass embodiments that are not required to perform the common utility.

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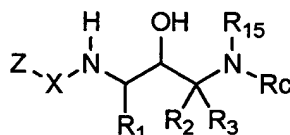
4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Mr. Bradley Crawford on February 28, 2006 a provisional election was made *without* traverse to prosecute the invention of Group I, claims 1-14 wherein R_c represents heteroaryl or heterocycloalkyl. Claims not drawn to the elected invention are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. The application has been amended as follows:

A. Claim 1 has been amended to read as follows:

--1. (Amended) A compound of the formula I:



(I)

or pharmaceutically acceptable salts thereof, wherein

Z is hydrogen, (C₃-C₇ cycloalkyl)₀₋₁(C₁-C₆ alkyl)-, (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkenyl)-, alkoxyalkoxyalkyl, (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkynyl)- or (C₃-C₇ cycloalkyl)-, wherein each of said groups is optionally substituted with 1, 2, or 3 R_Z groups, wherein 1 or 2 methylene groups within said (C₃-C₇ cycloalkyl)₀₋₁(C₁-C₆ alkyl)-, (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkenyl)-, (C₃-C₇ cycloalkyl)₀₋₁(C₂-C₆ alkynyl)- or (C₃-C₇ cycloalkyl)- groups are optionally replaced with -(C=O)-;

wherein R_Z at each occurrence is independently halogen, -OH, -SH, -CN, -CF₃, -OCF₃, C₁-C₆ alkoxy, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkoxy or -NR₁₀₀R₁₀₁;

where R₁₀₀ and R₁₀₁ are independently H, C₁-C₆ alkyl, phenyl, CO(C₁-C₆ alkyl) or SO₂C₁-C₆ alkyl;

X is -(C=O)-, -(C=S)-, -(SO₂)-;

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R_1 is C_1 - C_{10} alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, $-OH$, $=O$, $-SH$, $-CN$, $-CF_3$, $-OCF_3$, $-C_{3-7}$ cycloalkyl, $-C_1$ - C_4 alkoxy, amino, mono-dialkylamino, aryl, heteroaryl, and heterocycloalkyl, wherein each aryl group is optionally substituted with 1, 2 or 3 R_{50} groups;

R_{50} is selected from halogen, OH , SH , CN , $-CO-(C_1-C_4 \text{ alkyl})$, $-NR_7R_8$, $-S(O)_{0-2}-(C_1-C_4 \text{ alkyl})$, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_8 alkoxy, $-O$ -benzyl, alkenyloxy, alkoxyalkoxyalkoxy, and C_3-C_8 cycloalkyl;

wherein the alkyl, alkenyl, alkynyl, alkoxy and cycloalkyl groups are optionally substituted with 1 or 2 substituents independently selected from C_1-C_4 alkyl, halogen, OH , $-NR_5R_6$, CN , C_1-C_4 haloalkoxy, NR_7R_8 , and C_1-C_4 alkoxy;

R_5 and R_6 are independently H or C_1-C_6 alkyl; or

R_5 and R_6 and the nitrogen to which they are attached form a 5 or 6 membered heterocycloalkyl ring; and

R_7 and R_8 are independently selected from H ; $-C_1-C_4$ alkyl optionally substituted with 1, 2, or 3 groups independently selected from $-OH$, $-NH_2$, and halogen; $-C_3-C_6$ cycloalkyl; $-(C_1-C_4 \text{ alkyl})-O-(C_1-C_4 \text{ alkyl})$; $-C_2-C_4$ alkenyl; and $-C_2-C_4$ alkynyl;

wherein each heteroaryl is optionally substituted with 1 or 2 R_{50} groups;

wherein each heterocycloalkyl group is optionally substituted with 1 or 2 groups that are independently R_{50} or $=O$;

R_2 and R_3 are independently selected from

$-H$;

$-F$;

$-C_1-C_6$ alkyl optionally substituted with a substituent selected from $-F$, $-OH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_5R_6$;

$-(CH_2)_{0-2}-R_{17}$;

$-(CH_2)_{0-2}-R_{18}$;

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-C₂-C₆ alkenyl or C₂-C₆ alkynyl, wherein each is optionally substituted with an independent substituent selected from -F, -OH, , -C≡N, -CF₃ and C₁-C₃ alkoxy;

-(CH₂)₀₋₂-C₃-C₇ cycloalkyl, optionally substituted an independent substituent selected from -F, -OH, -C≡N, -CF₃, C₁-C₃ alkoxy and -NR₅R₆; or

wherein R₂, R₃ and the carbon to which they are attached form a carbocycle of three thru seven carbon atoms, wherein one carbon atom is optionally replaced by a group selected from -O-, -S-, -SO₂-, or -NR₇;

where R₁₇ at each occurrence is an aryl group selected from phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl and tetralinyl, wherein said aryl groups are optionally substituted with one or two groups that are independently

-C₁-C₃ alkyl; -C₁-C₄ alkoxy; CF₃; or

-C₂-C₆ alkenyl or -C₂-C₆ alkynyl each of which is optionally substituted with one substituent selected from F, OH, C₁-C₃ alkoxy; or

-halogen;

-OH;

-C≡N;

-C₃-C₇ cycloalkyl;

-CO-(C₁-C₄ alkyl);

-SO₂-(C₁-C₄ alkyl);

where R₁₈ is a heteroaryl group selected from pyridinyl, pyrimidinyl, quinolinyl, indolyl, pyridazinyl, pyrazinyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, oxazolyl, thiazolyl, furanyl, thienyl, pyrrolyl, oxadiazolyl or thiadiazolyl, wherein each of said heteroaryl groups is optionally substituted with one or two groups that are independently

-C₁-C₆ alkyl optionally substituted with one substituent selected from OH, C≡N, CF₃, C₁-C₃ alkoxy, and -NR₅R₆;

wherein R₁₅ is selected from hydrogen, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₁-C₆ alkoxy C₁-C₆ alkyl, hydroxy C₁-C₆ alkyl, halo C₁-C₆ alkyl, benzyl, -C(O)₂-benyl, and alkoxy carbonyl, wherein the alkyl and phenyl portion of each is unsubstituted or substituted with 1, 2, 3, or 4 groups independently selected from halogen, C₁-C₆ alkyl, hydroxy, C₁-C₆ alkoxy, NH₂, and -R₂₆-R₂₇;

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wherein R_{26} is selected from a bond, $-C(O)-$, $-SO_2-$, $-CO_2-$, $-C(O)NR_5-$, and $-NR_5C(O)-$,

wherein R_{27} is selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, aryl C_1-C_6 alkyl, heterocycloalkyl, and heteroaryl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, haloalkyl, hydroxyalkyl, $-NR_5R_6$, $-C(O)NR_5R_6$;

wherein R_C is selected from

heteroaryl;

heterocycloalkyl;

heteroaryl-aryl;

heteroaryl-heterocycloalkyl;

heteroaryl-heteroaryl;

heterocycloalkyl-heteroaryl;

heterocycloalkyl-heterocycloalkyl; or

heterocycloalkyl-aryl;

wherein each aryl group is optionally substituted with 1, 2, 3 or 4 R_{200} groups;

wherein each heteroaryl group is optionally substituted with 1, 2, 3, or 4 R_{200} ;

wherein each heterocycloalkyl is optionally substituted with 1, 2, 3, or 4 R_{210} ;

wherein R_{200} at each occurrence is independently selected from

$-C_1-C_6$ alkyl optionally substituted with 1, 2, or 3 R_{205} groups;

$-OH$;

$-NO_2$;

-halogen;

$-C\equiv N$;

$-CHO$;

$-(CH_2)_{0-4}-CO-NR_{220}R_{225}$;

$-(CH_2)_{0-4}-CO-(C_1-C_8 \text{ alkyl})$;

$-(CH_2)_{0-4}-CO-(C_2-C_8 \text{ alkenyl})$;

$-(CH_2)_{0-4}-CO-(C_2-C_8 \text{ alkynyl})$;

$-(CH_2)_{0-4}-CO-(C_3-C_7 \text{ cycloalkyl})$;

$-(CH_2)_{0-4}-(CO)_{0-1}\text{-aryl}$;

$-(CH_2)_{0-4}-(CO)_{0-1}\text{-heteroaryl}$;

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$-(CH_2)_{0-4}-(CO)_{0-1}$ -heterocycloalkyl;
 $-(CH_2)_{0-4}-CO_2R_{215}$;
 $-(CH_2)_{0-4}-SO_2-NR_{220}R_{225}$;
 $-(CH_2)_{0-4}-S(O)_{0-2}-(C_1-C_8 \text{ alkyl})$;
 $-(CH_2)_{0-4}-S(O)_{0-2}-(C_3-C_7 \text{ cycloalkyl})$;
 $-(CH_2)_{0-4}-N(H \text{ or } R_{215})-CO_2R_{215}$;
 $-(CH_2)_{0-4}-N(H \text{ or } R_{215})-SO_2-R_{220}$;
 $-(CH_2)_{0-4}-N(H \text{ or } R_{215})-CO-N(R_{215})_2$;
 $-(CH_2)_{0-4}-N(-H \text{ or } R_{215})-CO-R_{220}$;
 $-(CH_2)_{0-4}-NR_{220}R_{225}$;
 $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$;
 $-(CH_2)_{0-4}-O-(R_{215})$;
 $-(CH_2)_{0-4}-S-(R_{215})$;
 $-(CH_2)_{0-4}-O-(C_1-C_6 \text{ alkyl optionally substituted with 1, 2, 3, or 5 -F})$;
 $-C_2-C_6 \text{ alkenyl optionally substituted with 1 or 2 } R_{205} \text{ groups}$;
 $-C_2-C_6 \text{ alkynyl optionally substituted with 1 or 2 } R_{205} \text{ groups}$;
 and
 $-(CH_2)_{0-4}-C_3-C_7 \text{ cycloalkyl}$;
 wherein each aryl group included within R_{200} is optionally substituted with 1, 2, or 3 groups that are independently

$-R_{205}$,

$-R_{210}$ or

$-C_1-C_6 \text{ alkyl substituted with 1, 2, or 3 groups that are independently } R_{205} \text{ or } R_{210}$;

wherein each heterocycloalkyl group included within R_{200} is optionally substituted with 1, 2, or 3 groups that are independently R_{210} ;

wherein each heteroaryl group included within R_{200} is optionally substituted with 1, 2, or 3 groups that are independently

$-R_{205}$,

$-R_{210}$, or

$-C_1-C_6 \text{ alkyl substituted with 1, 2, or 3 groups that are independently}$

$-R_{205}$ or

$-R_{210}$;

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wherein R_{205} at each occurrence is independently selected from

- C₁-C₆ alkyl,
- C₂-C₆ alkenyl,
- C₂-C₆ alkynyl,
- C₁-C₆ haloalkoxy
- (CH₂)₀₋₃(C₃-C₇ cycloalkyl)
- halogen,
- (CH₂)₀₋₆-OH,
- O-phenyl,
- alkenyl-phenyl,
- SH,
- (CH₂)₀₋₆-C≡N,
- (CH₂)₀₋₆-C(=O)NR₂₃₅R₂₄₀
- CF₃,
- C(O)₂-benzyl,
- C₁-C₆ alkoxy, and
- NR₂₃₅R₂₄₀,

wherein R_{210} at each occurrence is independently selected from

- C₁-C₆ alkyl optionally substituted with 1, 2, or 3 R_{205} groups;
- C₂-C₆ alkenyl optionally substituted with 1, 2, or 3 R_{205} groups;
- C₂-C₆ alkynyl optionally substituted with 1, 2, or 3 R_{205} groups;
- halogen;
- C₁-C₆ alkoxy;
- C₁-C₆ haloalkoxy;
- NR₂₂₀R₂₂₅;
- OH;
- C≡N;
- C₃-C₇ cycloalkyl optionally substituted with 1, 2, or 3 R_{205} groups;
- CO-(C₁-C₄ alkyl);
- SO₂-NR₂₃₅R₂₄₀;
- CO-NR₂₃₅R₂₄₀;
- SO₂-(C₁-C₄ alkyl); and

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=O; wherein

wherein R_{215} at each occurrence is independently selected from

- C₁-C₆ alkyl,
- (CH₂)₀₋₂-(aryl),
- C₂-C₆ alkenyl,
- C₂-C₆ alkynyl,
- C₃-C₇ cycloalkyl,
- (CH₂)₀₋₂-(heteroaryl), and
- (CH₂)₀₋₂-(heterocycloalkyl);

wherein the aryl group included within R_{215} is optionally substituted with 1, 2, or 3 groups that are independently

-R₂₀₅ or

-R₂₁₀;

wherein the heterocycloalkyl group included within R_{215} is optionally substituted with 1, 2, or 3 R₂₁₀;

wherein each heteroaryl group included within R_{215} is optionally substituted with 1, 2, or 3 R₂₁₀;

wherein R_{220} and R_{225} at each occurrence are independently selected from

- H,
- C₁-C₆ alkyl,
- hydroxy C₁-C₆ alkyl,
- amino C₁-C₆ alkyl,
- halo C₁-C₆ alkyl,
- (CH₂)₀₋₂-(C₃-C₇ cycloalkyl),
- (C₁-C₆ alkyl)-O-(C₁-C₃ alkyl),
- C₂-C₆ alkenyl,
- C₂-C₆ alkynyl,
- aryl,
- heteroaryl, and
- heterocycloalkyl;

wherein the aryl, heteroaryl or heterocycloalkyl group included within R_{220} and R_{225} is optionally substituted with 1, 2, or 3 R₂₇₀ groups,

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wherein R_{270} at each occurrence is independently

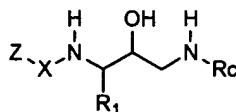
- R_{205} ;
- C_1-C_6 alkyl optionally substituted with 1, 2, or 3 R_{205} groups;
- C_2-C_6 alkenyl optionally substituted with 1, 2, or 3 R_{205} groups;
- C_2-C_6 alkynyl optionally substituted with 1, 2, or 3 R_{205} groups;
- halogen;
- C_1-C_6 alkoxy;
- C_1-C_6 haloalkoxy;
- $NR_{235}R_{240}$;
- OH;
- $C\equiv N$;
- C_3-C_7 cycloalkyl optionally substituted with 1, 2, or 3 R_{205} groups;
- CO-(C_1-C_4 alkyl);
- $SO_2-NR_{235}R_{240}$;
- CO- $NR_{235}R_{240}$;
- $SO_2-(C_1-C_4$ alkyl); and
- =O;

wherein R_{235} and R_{240} at each occurrence are independently

- H,
- C_1-C_6 alkyl; or
- phenyl.—

B. Claim 10 has been amended to read as follows:

--10. (Amended) A compound according to claim 1 of the formula II:



(II)

wherein Z is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_3-C_7 cycloalkyl, where each of said groups is optionally substituted with 1 or 2 R_z groups, wherein 1 or 2 methylene groups within said C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_3-C_7 cycloalkyl groups are optionally replaced with $-(C=O)-$;

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wherein R_Z at each occurrence is independently halogen, -OH, -CN, -CF₃, C₁-C₆ alkoxy, C₃-C₇ cycloalkyl, C₃-C₇ cycloalkoxy or -NR₁₀₀R₁₀₁;

where R₁₀₀ and R₁₀₁ are independently H, C₁-C₆ alkyl, phenyl, CO(C₁-C₆ alkyl) or SO₂C₁-C₆ alkyl;

wherein X is -C(=O)-;

wherein R₁ is C₁-C₁₀ alkyl optionally substituted with 1 or 2 groups independently selected from halogen, -OH, =O, -CN, -CF₃, -OCF₃, -C₃-C₇ cycloalkyl, -C₁-C₄ alkoxy, amino, mono-dialkylamino, aryl, heteroaryl or heterocycloalkyl, wherein the aryl group is optionally substituted with 1 or 2 R₅₀ groups;

where R₅₀ is halogen, OH, CN, -CO-(C₁-C₄ alkyl), -NR₇R₈, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₁-C₆ alkoxy and C₃-C₈ cycloalkyl;

where R₇ and R₈ are selected from H; -C₁-C₄ alkyl optionally substituted with 1, 2, or 3 groups selected from -OH, -NH₂ and halogen; -C₃-C₆ cycloalkyl; -(C₁-C₄ alkyl)-O-(C₁-C₄ alkyl); -C₂-C₄ alkenyl; and -C₂-C₄ alkynyl;

wherein R_C is selected from

heteroaryl; or

heterocycloalkyl;

where the heteroaryl group is optionally substituted with 1, 2, 3, or 4 R₂₀₀ groups; and

where the heterocycloalkyl group is optionally substituted with 1, 2, 3, or 4 R₂₁₀ groups.--

C. Claim 11 has been amended to read as follows:

--11. (Amended) A compound according to claim 10, wherein

Z is -C₁-C₆ alkyl;

R₁ is C₁-C₁₀ alkyl substituted with 1 phenyl group, where the phenyl group attached to the alkyl is optionally substituted with 1 or 2 R₅₀ groups, where each R₅₀ is independently halogen, OH, CN, or C₁-C₆ alkyl; and

R_C is heteroaryl, where the heteroaryl group is optionally substituted with 1 or 2 R₂₀₀ groups.--

D. Claim 12 has been amended to read as follows:

--12. (Amended) A compound according to claim 1 which is

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[[(4R)-6-isopropyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}propyl]acetamide;

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N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(((4S)-6-isopropyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino)propyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]-2-hydroxypropyl)acetamide;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-2-methylamino-acetamide;

2-Amino-N-[1-(3,5-difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[6-ethyl-2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-4-yl]amino]-2-hydroxypropyl)acetamide;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-3-methyl-butylamide;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-3-hydroxy-2,2-dimethyl-propionamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,2-dioxido-3,4-dihydro-1,2-benzoxathiin-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-iodo-3,4-dihydro-2H-chromen-4-yl)amino]propyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(((4S)-6-iodo-3,4-dihydro-2H-chromen-4-yl)amino)propyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(((4R)-6-iodo-3,4-dihydro-2H-chromen-4-yl)amino)propyl)acetamide;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-3-hydroxy-propionamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-2,2-dioxido-3,4-dihydro-1,2-benzoxathiin-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-2,2-dioxido-3,4-dihydro-1,2-benzoxathiin-4-yl)amino]-2-hydroxypropyl)acetamide;

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N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[4-(3-ethylphenyl)tetrahydro-2H-pyran-4-yl]amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[4-(3-ethyl-3,4-dihydro-2H-chromen-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[4-(3-ethyl-3,4-dihydro-2H-chromen-4-yl)amino]-2-hydroxypropyl)acetamide;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-3-hydroxy-butyramide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-3,4-dihydro-1H-isothiochromen-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino]propyl)acetamide;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-2-phenyl-acetamide;

{[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]carbamoyl}-methyl}-methyl-carbamic acid tert-butyl ester;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-2-methyl-2-methylamino-propionamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-2,2-dioxido-3,4-dihydro-1H-2,1-benzothiazin-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-2,2-dioxido-3,4-dihydro-1H-2,1-benzothiazin-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-3-methyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-3-methyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[(6-ethyl-1-methyl-1,2,3,4-tetrahydroquinolin-4-yl)amino]-2-hydroxypropyl)acetamide;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-2-(1H-imidazol-4-yl)-acetamide;

N-[1-(3,5-Difluoro-benzyl)-3-(6-ethyl-2,2-dioxo-2 λ^6 -isothiochroman-4-ylamino)-2-hydroxypropyl]-propionamide;

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N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[1-(4-ethylpyridin-2-yl)cyclopropyl]amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[[(4S)-6-(1H-pyrrol-3-yl)-3,4-dihydro-2H-chromen-4-yl]amino]propyl]acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-isopropyl-3,4-dihydro-2H-chromen-4-yl)amino]propyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[1-(3-ethylphenyl)-2-(5-methyl-1,3-oxazol-2-yl)ethyl]amino]-2-hydroxypropyl)acetamide hydrochloride;

N-[(1S,2R)-1-(3,5-difluorobenzyl)-3-(3,4-dihydro-2H-chromen-4-ylamino)-2-hydroxypropyl]acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[[(4S)-6-isobutyl-3,4-dihydro-2H-chromen-4-yl]amino]propyl]acetamide;

N-[(1S,2R)-3-[[[(4S)-6-cyano-3,4-dihydro-2H-chromen-4-yl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[[[(4S)-6-neopentyl-3,4-dihydro-2H-chromen-4-yl]amino]propyl]acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-neopentyl-3,4-dihydro-2H-chromen-4-yl)amino]propyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[[(4R)-6-(2,2-dimethylpropyl)-3,4-dihydro-2H-chromen-4-yl]amino]-2-hydroxypropyl]acetamide;

N-[(1S,2R)-3-[[4-(3-tert-butylphenyl)tetrahydro-2H-pyran-4-yl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[6-(2,2-dimethylpropyl)-1,2,3,4-tetrahydroquinolin-4-yl]amino]-2-hydroxypropyl)acetamide;

N-[(1S,2R)-3-[[[(4S)-6-(2,2-dimethylpropyl)-3,4-dihydro-2H-chromen-4-yl]amino]-1-(3-fluorobenzyl)-2-hydroxypropyl]acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[5-(2,2-dimethylpropyl)-2-(1H-imidazol-1-yl)benzyl]amino]-2-hydroxypropyl)acetamide;

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-[[6-(2,2-dimethylpropyl)-4-methyl-3,4-dihydro-2H-chromen-4-yl]amino]-2-hydroxypropyl)acetamide;

N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({1-[3-(3-thienyl)phenyl]cyclohexyl}amino)propyl]acetamide;

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N-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({1-[4-(2,2-dimethylpropyl)pyridin-2-yl]cyclopropyl}amino)-2-hydroxypropyl]acetamide; or a pharmaceutically acceptable salt thereof.--

E. Claim 14 has been amended to read as follows:

-- 14. (Amended) A method of treating a subject who has Alzheimer's disease (AD); treating subjects with mild cognitive impairment (MCI); treating Down's syndrome; treating subjects who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type; treating cerebral amyloid angiopathy, treating other degenerative dementias; treating dementia associated with Parkinson's disease, progressive supranuclear palsy, or cortical basal degeneration; treating diffuse Lewy body type AD; and frontotemporal dementias with parkinsonism (FTDP), the method comprising administering a therapeutically effective amount of a compound or salt of claim 1 to a person in need of such treatment.

F. New claim 15 has been added as follows:

--15. (New) A pharmaceutical composition comprising a compound or salt of claim 1 and at least one pharmaceutically acceptable carrier, solvent, adjuvant or diluent.

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance:

7. Applicants preserve the right to file divisional applications drawn to the non-elected subject matter.
8. Claim 14 (method of treating) has been rejoined with the claims 1-13. As such, new linking claim 15 has been added. Support of this claim is found at page 11, lines 20-24.

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9. The claims have been amended to elected subject matter wherein R_c represents heteroaryl or heterocycloalkyl. The changes are not made to avoid any rejections based upon prior art.

10. Reference N (WO 96/39385) has been cited to show the state of the art. The differences between the prior art compound and the instantly claimed compound is the 1) the Z radical cannot represent a heterocyclic moiety and 2) R₂ and R₃ do not form -(C=O)-. There is neither teaching nor suggestion to modify the prior art compounds to derive those instantly claimed. Accordingly, the claims are deemed patentable therefrom.

11. The rejection based upon obviousness-type double patenting over Application No. 10/313,849 is withdrawn. The claimed subject matter is patentably distinct.

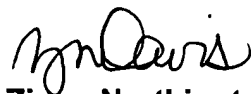
12. Based upon the amendment filed May 26, 2005, the rejections set forth in the Office Action mailed February 24, 2005 under 35 U.S.C. §112, 1st and 2nd paragraph are withdrawn.

13. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zinna N. Davis whose telephone number is 571-272-0682.

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15. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Zinna Northington Davis
Primary Examiner
Group 1600-AU 1625